REMARKS

Claims 2-22 are pending and under consideration. By the present communication, claims 2, 16, and 21 have been amended to define Applicants' invention with greater particularity, and claims 20 and 22 have been canceled without prejudice. The claim amendments add no new matter, being fully supported by the Specification and original claims. Accordingly, claims 2-19 and 21 will be pending.

Rejection under 35 U.S.C. § 112, Second Paragraph

Claims 16 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant respectfully traverses this rejection.

The Office Action alleges that claim 16 is confusing by reciting "the anticoagulant is heparin" because heparin is not an anticoagulant that is administered orally. Applicant has amended claim 16 to substitute "warfarin" for "heparin." Support for the amendment may be found at page 7, line 30 of the specification. Accordingly, Applicants respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. § 112, First Paragraph

Applicants respectfully traverse the rejection of claims 20 and 22 under 35 U.S.C. § 112, first paragraph, on the grounds that the Specification allegedly does not describe the claimed invention so as to reasonably convey to those of skill in the art that the inventor has possession of the invention at the filing date of the application. To reduce the issues and advance prosecution, claims 20 and 22 have been canceled without prejudice. Accordingly, Applicants respectfully request withdrawal of the rejection.

Rejection Under 35 U.S.C. § 102(a)

The rejection of claims 2-22 under 35 U.S.C. § 102(a) as allegedly anticipated by Sun et. al. (*Blood*, 83, 3120, 1994), is respectfully traversed. As stated above, claims 20 and 22 have been canceled, rendering the rejection moot as to claims 20 and 22.

To anticipate an invention, each and every element of a claim must be found in a single prior art reference. MPEP § 2131; *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628,631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The invention methods for diagnosing a subject as having or as being at risk for having a thrombotic disorder associated with activated protein C (APC)-resistant factor V or Va, as defined by amended claims 2 and 18, distinguish over the disclosure of Sun et al. by requiring that the test sample is *initially* diluted from about 1/40 to 1/80. Support for the amendment may be found at page 11, lines 22-23 of the specification. Sun et al. fail to teach a method in which the test sample (i.e., plasma from a subject) is initially diluted 1/40 to 1/80. Thus, Sun et al. fail to disclose each and every aspect of the invention methods for diagnosing a subject as having or as being at risk for having a thrombotic disorder associated with activated protein C (APC)-resistant factor V or Va, as would be required to support a rejection for anticipation under 35 U.S.C. § 102. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection for alleged anticipation of claims 2-19 and 21 over the disclosure of Sun et al.

Rejection Under 35 U.S.C. § 103(a)

The rejection of claims 18-19 under 35 U.S.C. § 103(a) as allegedly being obvious over Dahlback (WO 94/17415) in view of The Merck Manual and the PDR, is respectfully traversed. The burden of proof in establishing a *prima facie* case of obviousness under § 103 clearly rests with the Patent Office. *In re Piasecki,* 745 F.2d 1468, 1472 (Fed. Cir. 1984). In establishing a *prima facie* case, the Patent Office, among other things, must show that (1) the prior art would have suggested to those of ordinary skill in the art that they should make the claimed invention and (2) that the prior art would have revealed a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). "Both the suggestion and the reasonable expectation of success must be found in the prior art, not in the applicant's

disclosure." *Id.* Thus, "particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed." *In re Kotzab*, 217 F.3d 1365, 1371 (Fed. Cir. 2000). Further, when relying on the knowledge of persons of ordinary skill in the art, the Patent Office must "explain what specific understanding or technological principle within the knowledge of one of ordinary skill in the art would have suggested the combination." *In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998).

The Examiner alleges that Dahlback teaches a like assay, in which there is a dilution of a sample into Factor V-deficient plasma (Office Action, page 5). Applicants have amended claim 18 to include the limitation that the test sample is *initially* diluted from about 1/40 to 1/80. It is respectfully submitted that Dahlback is silent regarding initial dilution of the test sample to such an extent. Likewise, the teachings of The Merck Index and the PDR fail to overcome the deficiencies of Dahlback with regard to initially diluting the test sample. Thus, it would not have been obvious to one of ordinary skill in the art that the method assays for diagnosing a subject as having or as being at risk for having a thrombotic disorder associated with activated protein C (APC)-resistant factor V or Va would work at the initial dilutions taught in the subject application.

Applicants respectfully submit that Dahlback in combination with The Merck Index and/or the PDR, is not sufficient to establish *prima facie* obvious of the invention methods, as defined by amended claim 18. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the above remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

Respectfully submitted,

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